UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,596	10/18/2005	Rena Nishizawa	Q90950	4644

65565 7590 04/05/2007

SUGHRUE-265550
2100 PENNSYLVANIA AVE. NW
WASHINGTON, DC 20037-3213

EXAMINER	
MURRAY, JEFFREY H	
ART UNIT	**PAPER NUMBER**
1609	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,596	NISHIZAWA, RENA	
	Examiner	Art Unit	
	Jeffrey H. Murray	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/9/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *10-19* is/are withdrawn from consideration.

5)☐ Claim(s) *8* is/are allowed.

6)☒ Claim(s) *1-7 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/18/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-19 are pending in this application.

Election/Restrictions

1. Applicant's election of Group VIII in Paper No. 18 is acknowledged. The applicant has selected their election expressly without traverse. The restriction requirement is deemed proper and therefore made FINAL. Claims 10-19 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Applicants are expected to limit the claims in the scope of the elected subject matter.

Specification

2. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any of the errors of which applicant may become aware of in the specification.

Claim Objections

3. Claim 1 is objected to for being vague and indefinite. Neither "ring A" nor "ring B" contain an article in front of it. It is suggested that applicant insert the word "a" before "ring A" and the first "ring B" in Claim 1. Also, the word "the" should appear before the second "ring B." Appropriate correction is required.

4. Claim 4 is objected to for being vague and indefinite. It is suggested that applicant insert the word "the" before the words "ring B" in Claim 4. Appropriate correction is required.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Teranishi et. al.; EP 70,171. See CA 1983:470751 where the instantly claimed compounds read on the reference compounds. See either CA registry number 85732-34-9, i.e., the corresponding ring A is a tetrahydropyrimidin-2-(1H)-one, ring B is phenyl, R^1 is a benzyl group, R^2 is a methyl group, and R^5 is H; or CA registry number 85732-35-0, i.e., the corresponding ring A is a tetrahydropyrimidin-2-(1H)-one, ring B is a phenyl group, R^1 and R^5 are H and R^2 is a methyl group.

Claims 1-7, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated Kyowa Hakko Kogyo Co.; JP 59,059,685. See CA 1984:510946 where the instantly claimed compounds read on the reference compounds. See either CA registry number 85732-35-0, i.e., the corresponding ring A is a tetrahydropyrimidin-2-(1H)-one, ring B is phenyl, R^1 is H, R^2 is a methyl group, and R^5 is H; or CA registry number 85732-42-9, i.e., the corresponding ring A is a tetrahydropyrimidin-2-(1H)-one, ring B is an *m*-chlorophenyl group, R^1 is a methyl group, R^2 is an ethyl group and R^5 is H.

Claims 1-7, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Takai et. al.; Chem.Pharm.Bull. 36(12), 4659-70. See CA 1989:407312 where the instantly claimed compounds read on the reference compounds. See either CA registry number 85732-35-0, i.e.,

the corresponding ring A is a tetrahydropyrimidin-2-(1H)-one, ring B is phenyl, R^1 is H, R^2 is a methyl group, and R^5 is H; or CA registry number 121061-07-2, i.e., the corresponding ring A is a tetrahydropyrimidin-2-(1H)-one, ring B is an *m*-chlorophenyl group, R^1 is a benzyl group, R^2 is a methyl group and R^5 is H.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-7, and 9 are rejected under 35 U.S.C. 102(a) as being anticipated by Uesaka et. al.; WO 2003028732. See CA 2003:282402 where the instantly claimed compounds read on the reference compounds. See either CA registry number 508240-62-8, i.e., the corresponding ring A is a tetrahydropyrimidin-2-(1H)-one, ring B is phenyl, R^1 is H, and R^2 and R^5 are a methyl group; or CA registry number 508240-61-7, i.e., the corresponding ring A is a tetrahydropyrimidin-2-(1H)-one, ring B is phenyl, R^1 is a benzyl group and R^2 and R^5 are a methyl group.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7, and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Chaturvedula et. al.; US 2004/0204397. See CA 2003:991516 where the instantly claimed

compounds read on the reference compounds. See either CA registry number 635713-68-7, i.e., the corresponding ring A is a tetrahydropyrimidin-2-(1H)-one, ring B is phenyl, R^1, R^2, and R^5 are H; or CA registry number 635713-67-6, i.e., the corresponding ring A is a tetrahydropyrimidin-2-(1H)-one, ring B is phenyl, R^1 is a benzyl group and R^2 and R^5 are H.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-7, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirzadegan et. al.; in view of Poindexter et. al. (WO 01/13917) and Berger et. al. (US 3,301,857).

The current application recites a variety of specific spiropiperidine compounds. In this application the spiro ring was restricted to a tetrahydropyrimidin-2(1*H*)-one, which was attached

at the 4-position of the piperidine. All of the compounds listed in the claims had this core, with an optional ring attached to the tetrahydropyrimidin-2(1*H*)-one.

In medicinal chemistry, bioisosteres are substituents or groups with similar physical or chemical properties that may impart similar biological properties to a chemical compound. In drug design, the purpose of exchanging one bioisostere for another is to enhance that desired biological or physical properties of a compound without making significant changes in chemical structure (Ann.Rpts.Med.Chem. **21**, 283-291).

The published reference teaches a group of compounds which are similar in scope to the current application. Throughout Mirzadegan et. al., (chart, p. 25565) similar spiropiperidine structures are seen which teach these compounds as being used for a similar purpose as the proposed application. That is, the spiropiperidine compounds were synthesized and tested as a novel class of chemokine receptor antagonists.

Mirzadegan et. al. has an identical core structure to the current patent application with one major difference. Mirzadegan et. al. has a 1,3-oxazinan-2-one ring as the spiro ring stemming from the piperidine whereas the current application has in its place a tetrahydropyrimidin-2(1*H*)-one ring. A phenyl ring is fused to the 1,3-oxazinan-2-one ring in the same fashion as a B ring can be fused to the A ring in the current application.

The patent reference, Poindexter et. al., page 3-6, and Berger et. al. (page 2, col. 3, para. 2) describes in detail the synthesis of spiropiperidines as well. These compounds contain as the spiro ring a 3,4-dihydroquinolin-2(1*H*)-one, or another way of describing it is to say the spiro A ring is a piperidin-2-one while the fused B ring is a phenyl ring.

Poindexter et. al. and Berger et. al. both synthesized similar spiropiperidine compounds. Poindexter et. al. did so to develop an NPY antagonist. These spiropiperidines contained an A ring that was a piperidon-2-one ring. In comparing the compounds synthesized in these two patents to the current application, these ring systems lack a nitrogen in the 4-position on the piperid-2-one ring.

The Mirzadegan et. al. patent reference also synthesized similar spiropiperidine compounds. Here though, Mirzadegan et. al. did so to for the same purpose as the applicants, that is, to find a chemokine receptor antagonist. The difference structurally between the compounds of the Mirzadegan et. al. patent reference and the current application is a single atom. Mirzadegan et. al. reference and the current application both contain spiropiperidine ring systems. For Mirzadegan et. al., attached in spiro fashion to this ring is a cyclic carbamate. That is, a 6-membered ring in which an oxygen is in the 2-position, a carbonyl in the 3-position and a nitrogen in the 4-position, with a phenyl ring fused to the 5 and 6 position. The applicants on the other hand, are attempting to patent a very similar set of compounds. One in which also contains a 6-membered ring attached in spiro fashion to the piperidine. Here though, the ring is a cyclic urea. That is, a nitrogen is in the 2-position, a carbonyl in the 3-position and another nitrogen in the 4-position. Note that except for this single atom difference, the compounds of Mirzadegan et. al would read on this application as prior art as a 102(b) reference.

Often, in an attempt to further strengthen a compound's activity, researchers will replace an oxygen with a nitrogen or vice versa, to determine possible binding effects and atom interactions. It is quite common to see research where a pyridine, pyrimidine, piperidine, and an imidazole all are inserted into a compound in the same position to determine if there would be

any altering of activity, better binding, steric effects, etc. Here, spiropiperidine compounds where the 2nd spiro ring was a 6-membered ring were already well known in the art. Also well known in the art were 6-membered rings which contained a cyclic amide, such as the aforementioned piperid-2-one. A compound which also misses defeating applicants claims by a single atom, a nitrogen in the 4-position. By looking at Mirzadegan et. al. in light of Poindexter et. al. and Berger et. al., replacing the oxygen in Mirzadegan et. al.'s spiropiperidine compounds with a nitrogen to act as a bioisostere in an attempt to obtain better antagonist activity seems obvious.

It would have been obvious to one skilled in the arts at the time of the invention to be motivated to replace either an 1,3-oxazinan-2-one or a piperidin-2-one moiety with a pyrimid-2-one moiety. Poindexter et. al. and Berger et. al. combined with Mirzadegan et. al. show the necessary teachings that suggest replacing a 1,3-oxazinan-2-one or a piperidin-2-one moiety, and one would have been motivated to substitute a pyrimid-2-one to enhance activity and afford a positive benefit from the replacement.

Conclusion

10. Claims 1-7, and 9 are rejected.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is 571-272-9023. The examiner can normally be reached on M-F 7:30-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Cecilia Tsang can be reached at 571-272-0562 or Janet Andres can be reached at 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jeffrey H. Murray

CECILIA TSANG
SUPERVISORY PATENT EXAMINER